CHARACTERIZATION OF ANTIOXIDANT, ANTIMICROBIAL AND ANTI-AGING PROPERTIES OF ALPHA-MANGOSTIN FROM MANGOSTEEN PERICARP (*GARCINIA MANGOSTANA* LINN.)

TENG YI SIEW

A thesis submitted in fulfilment of the
requirements for the award of the degree of
Master of Engineering (Bioprocess)

Faculty of Chemical and Energy Engineering
Universiti Teknologi Malaysia

AUGUST 2017

Dedicated to my beloved family and friends.

ACKNOWLEDGEMENTS

I would like to express my heartfelt appreciation to my supervisor Dr Mariani Abdul Hamid, for her continuous guidance, support and encouragement throughout this research. Thank you for giving me the opportunity to work on this interesting project.

I would also like to thank to Institute of Bioproduct Development (IBD) and Universiti Teknologi Malaysia especially to the Department of Bioprocess Engineering, Faculty of Chemical Engineering (FKK) for providing a good environment and facilities to complete this project. Thanks also to the Perpustakaan Sultanah Zanariah librarian for enabling me to get access to all relevant literatures.

I wish to thank to all of my colleagues in the Institute of Bioproduct Development, especially Master Student Norshamiza binti Abu Bakar, Tan Ying Fang and PhD student Koay Yin Shin for their inspirations and support.

Last but not least, my deepest gratitude goes to my family for support, patience and understanding throughout the period of the study and to my friends for their encouragement during this study.

ABSTRACT

In recent years, public interest on skincare cosmetics has shifted from synthetic to natural product due to adverse reactions of synthetic skincare cosmetics. In present study, α-mangostin from pericarp extract of *Garcinia Mangostana* Linn was evaluated for its *in vitro* antioxidant, antimicrobial and anti-aging properties. Determination of total antioxidant capacity was carried out by DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity and ABTS (2,2-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid)) assay. The antimicrobial activity was assessed using Minimum Inhibitory Concentration (MIC) test against: three selected bacteria strains *Staphylococcus aureus* (*S.aureus*), *Propionibacterium acnes* (*P. acnes*) and *Pseudomonas aeruginosa* (*P. aeruginosa*); and two fungi strains *Trichophyton rubrum* (*T. rubrum*) and *Trichophyton mentagrophytes* (*T. mentagrophytes*). Meanwhile, Bromide MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium) assay, collagen estimation assay and anti-collagenase assay were carried out to investigate the *in vitro* anti-aging effect of α-mangostin on human skin fibroblast cells. The α-mangostin exhibited high anti-oxidant capacity with IC_{50} (Half maximal inhibitory concentration) value of 0.0288 mg and 0.4637 mg, using ABTS assay and DPPH assay, respectively. The MIC values against test bacteria ranged between 0.156 mg/ml and 10 mg/ml whereas against fungi, MIC ranged from 2.5 mg/ml to 10 mg/ml. The following is the order of antimicrobial efficiency of α-mangostin on selected test microbes: *S. aureus* > *P. acnes* > *T. rubrum* > *P. aeruginosa* > *T. mentagrophytes*. Meanwhile, α-mangostin significantly restored the synthesis of pro-collagen on UVB (Ultraviolet B) irradiated human skin fibroblast in a dose dependent manner. The collagen content was increased by 3-fold upon treatment of 2 µg/ml α-mangostin. Extract of α-mangostin also showed good inhibitory effect on collagenase at 89.89 ±1.52%. Based on the outcomes, the recommended α-mangostin concentration to be formulated in cosmetic product is ranged from 1-2 µg/ml.

ABSTRAK

Dalam tahun kebelakangan ini, minat orang awam terhadap kosmetik telah beralih daripada produk sintetik kepada produk semula jadi akibat kesan sampingan produk sintetik. Dalam kajian ini, α-mangostin daripada ekstrak perikarpa *Garcinia Mangostana* Linn telah dinilai untuk mengkaji sifat-sifat antioksida, antimikrob dan anti-penuaan in vitro. Penentuan jumlah kapasiti antioksida telah dijalankan menggunakan DPPH (2,2-Diphenyl-1-picrylhydrazyl) dan ABTS (2,2-azino-bis (asid 3-ethylbenzothiazoline-6-sulphonic)). Aktiviti antimikrob dinilai menggunakan ujian kepekatan perencatan minimum (MIC) terhadap: tiga jenis bakteria terpilih *Staphylococcus aureus* (*S.aureus*), *Propionibacterium acnes* (*P. acnes*) dan *Pseudomonas aeruginosa* (*P. aeruginosa*); dan dua jenis kulat *Trichophyton rubrum* (*T. rubrum*) dan *Trichophyton mentagrophytes* (*T. mentagrophytes*). Sementara itu, ujian Bromide MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium), anggaran kolagen dan anti-kolagenase telah dijalankan untuk menyiasat kesan anti-penuaan daripada α-mangostin pada sel-sel *fibroblast* kulit manusia. Ekstrak α-mangostin mencatatkan nilai anti-oksida yang tinggi dengan nilai IC_{50} (Half maximal inhibitory concentration) sebanyak 0.0288 mg/ml dan 0.4637 mg/ml, masing-masing menggunakan ujian ABTS dan DPPH. Nilai MIC terhadap bakteria adalah antara 0.156 mg/ml dan 10 mg/ml sebaliknya terhadap kulat, nilai MIC adalah dari 2.5 mg/ml hingga 10 mg/ml. Berikut adalah tertib kecekapan ujian antimikrob oleh α-mangostin terhadap bahan uji mikrob terpilih: *S. aureus*> *P. acnes*> *T. rubrum*> *P. aeruginosa*> *T. mentagrophytes*. Sementara itu, α-mangostin dapat memulihkan sintesis pro-kolagen pada radiasi UVB (Ultraviolet B) pada sel *fibroblast* kulit manusia bergantung kepada dos. Kandungan kolagen telah meningkat sebanyak 3 kali ganda melalui dos rawatan 2 µg/ml α-mangostin. Ekstrak α-mangostin juga menunjukkan kesan perencatan yang baik terhadap kolagenase pada 89.89 ± 1.52%. Berdasarkan hasil kajian ini, cadangan kepekatan α-mangostin untuk digunakan di dalam produk kosmetik anti-penuaan adalah di antara 1-2 µg/ml.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AP-1	Activator Protein 1
ABTS	2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)
ATCC	American Type Culture Collection
DPPH	2,2-diphenyl-2-picrylhydrazyl
CAGR	Compound Annual Growth Rate
C_6-C_3-C_6	Tricyclic Aromatic System
CO_2	Carbon Dioxide
COX-2	Cyclooxygenase-2
DMEM	Dulbecco’s Modified Eagle Medium
DMSO	Dimethyl Sulfoxide
DNA	Deoxyribonucleic acid
DQ	Dye-quenched
e^-	electron
EDTA	Ethylenediaminetetraacetic acid
FBS	Fetal Bovine Serum
Fe^{2+}	Iron (II) cation
Fe^{3+}	Iron (III) cation
GML	*Garcinia Mangostana* Linn
g	gram
g/L	gram per liter
h	hour
HAT	Hydrogen Atom Transfer
HSF	Human Skin Fibroblast
HPLC	High Performance Liquid Chromatography

HPLC-DAD	High Performance Liquid Chromatography with Diode-Array Detection
IC50	Half Maximal Inhibitory Concentration
IL-1α	Interleukin 1 alpha
IL-6	Interleukin 6
LDL	Low Density Lipoproteins
µg/ml	microgram per milliliter
µl	microliter
µm	micrometre
cm^2	square centimeter
cfu/ml	coloning forming units per milliliter
min	minutes
mg	milligram
mg/ml	milligram per milliliter
MJ/cm^2	millijoule per square centimeter
ml	milliliter
mm	millimeters
M	molar
ppm	part per million
v/v	volume per volume
MAP	Mitogen-activated protein
MIC	Minimum Inhibitory Concentration
mRNA	Messenger Ribonucleic acid
MMP	Matrix Metalloproteinase
MMP-1	Collagenases
MMP-2	Gelatinase A
MMP-3	Stromelysin
MMP-9	Gelatinase
MOPS	3-(N-morpholino) propanesulfonic acid
MTT	3-(4,5-Dimethylthiazol-2-Yl)-2,5-Diphenyltetrazolium Bromide
nm	nanometer
NCCLS	National Committee for Clinical Laboratory Standards
NF-Kb	Nuclear factor –Kb

NMR	Nuclear Magnetic Resonance
$NO^{\bullet}$	Nitric Oxide Radicals
O_2	Oxygen Molecule
$O_2^{\bullet-}$	Superoxide Anion Radicals
$OH^{\bullet}$	Hydroxyl Radical
H^+	Hydrogen Atom
H_2O	Water
H_2O_2	Hydrogen Peroxide
pH	Potential of Hydrogen
PDA	Photodiode Array Detector
RMPI	Roswell Park Memorial Institute
ROS	Reactive Oxygen Species
SD	Standard Deviation
SDA	Sabouraud Dextrose Agar
SOD	Superoxide Dismutase
TGF-β	Transforming growth factor beta
TPA	12-O-tetradecanoyl phorbol-13-acetate
UV	Ultraviolet
([Gly-X-Y]n)	Repeat Unit of collagen triple helix

LIST OF SYMBOLS

*	Asterisk
˚C	Degree Celcius
$	Dollar Sign
=	Equals Sign
α	Greek Small Letter Alpha
β	Greek Small Letter Beta
γ	Greek Small Letter Gamma
κ	Greek Small Letter Kappa
<	Less than
×	Multiplication Sign
%	Percent Sign
±	Plus-Minus Sign
®	Registered Sign
/	Solidus
™	Trade Mark Sign

CHAPTER 1

INTRODUCTION

1.1 Research Background

In recent years, the global cosmeceutical industry has emerged tremendously owing to the high demand for beauty products that offer a pharmaceutical therapeutic benefit. According to a report from Business Wire (2014), the global cosmeceutical market was estimated at US $35 Billion and is expected to increase around 7% for the compound annual growth rate (CAGR) during 2013 to 2018. Among it, skin care products own the most important segment along with people of diverse age group. In particular, antibacterial ingredients mostly designated to teenage populations meanwhile antioxidants and anti-aging ingredients formulated products are subjected to people entering the middle stage of life. This report justify that people tend to invest extensively on maintaining youthful and elegance appearance, hence contribute to the massive increment of the cosmeceutical market (William Reed Business Media, 2014).

Nowadays, regardless of the therapeutic advantages of the cosmeceutical product in the market, consumers are more concerned on the safety and hazardous effect. These concerns are due to synthetic cosmetics that have been reported to cause harmful effect to the skin. For instance, bentonite, parabens, propylene glycol, and ethylene glycol are some common hazardous chemicals used in cosmetics which could cause irritation, photo toxicity, contact allergy, contact dermatitis and serious health conditions if sufficient is absorbed by the body (Chermahini *et al*., 2011). In turn, public interest has shifted interest from synthetic cosmetics to natural one.

Several medicinal plants are known to be important sources of biologically active chemical substances such as tannins, phenolics, flavonoids, alkaloids, glycosides, saponins, and other chemical compounds which have curative properties (Abalaka and Oyewole, 2011). These biologically active constituents often displayed antioxidant and antimicrobial properties which can help our immune system against both cellular oxidation reactions and pathogens. Over the past decades, mangosteen plant parts have been studied and shown to contain high amount of xanthones which then learned to have potential biological activities in *in vitro* systems (Obolskiy *et al*., 2009). Natural antioxidants from plants play significant roles as radical scavengers against oxygen-centered free radicals and other reactive oxygen species (ROS) and hence resist the cellular oxidative damage either in intrinsic or extrinsic way (Ozsoy *et al*., 2008). As such, it is utmost important to discover safe and potent antioxidants to decrease free radical production in skin as well as to preserve youthful appearance.

Oxidative damage can occur intrinsically and extrinsically which, eventually lead to skin aging. When UV was exposed to skin, superoxide radical is generated and activates a number of phosphorylase mediated kinases, leading to the activation of signal transduction pathways throughout the epidermis. Matrix metalloproteinases (MMP) is a family of zinc-containing proteinases which specifically degrade the extracellular matrix proteins that comprise connective tissue. Among the family of MMPs which initiate the degradation of Type I collagen (90% of its dry weight), MMP-1 play significant role in collagen fragmentation and thus initiate the appearance of aged human skin (Murina *et al*., 2012). According to Wlaschek *et al*. (2001) and Kang *et al*. (2001), the collagen fragmentation activity is also increases with a positive dose-response relationship with UV radiation. Hereby, the antioxidants which can down regulate the matrix metalloproteinase caused by ROS will enhance the anti-aging mechanism and promote the restoration of collagen in the epidermis.

Aging occurs across different organs tissues and cells, while the aging signs of internal organs are masked from the ambient “eyes”, the skin provides first obvious marks of the passing time (Ganceviciene *et al*., 2012). Therefore, skin anti-aging strategies which attempted to reverse the dermal and epidermal signs of photo- and chronological aging have been a subject undergoing intense study. In most of the skin anti-aging therapy, the mainspring is to achieve a healthy, smooth, blemish-free, translucent and resilient skin (Vedamurthy, 2006). In order to diminish presentation of aging, it encounter both intrinsic and extrinsic factors, namely from life to the immune, genetic, emotional and health status in general. The approaches for skin anti-aging can be grouped in few, such as cosmetological care, topical medicine agents or topical agents, invasive procedures, systemic agents, avoiding of exogenous factors of aging, correction of life style and habits, and preventive medicine (Ganceviciene *et al*., 2012). In this particular study, it focuses on the exploration of antioxidant as the components to control collagen degradation by reducing the concentration of free radicals in the tissues.

Skin infections by bacterial and fungal are sometimes being thought as mild diseases when compared with diseases that cause significant mortality (Hay *et al*., 2006). However, skin problems often appeared over the body surface, for instance the outer layers of the skin, the nails and hair, affecting the facial appearance and consequently the social relations. Specifically with the advancement of knowledge on cosmetic arena, people tend to seek for cosmeceuticals which can provide safe dermal applications with minimum side effects (Kumari and Khurana, 2013). Therefore, it is a great need to investigate natural component such as α-mangostin for its antimicrobial activities against bacterial and fungal species to provide new discovery of active ingredients from natural products to be formulated in the cosmetic product.

1.2 Problem Statement

Due to the public awareness on the safety of cosmeceutical products, they are keen to shift from synthetic cosmetics to natural ones. This is mainly due to the adverse reactions resulted from the synthetic skincare cosmetics, for instance allergic contact dermatitis, phototoxic and photo-allergic reactions, and irritant contact dermatitis. In the present study, mangosteen pericarp (*Garcinia mangostana* Linn) was chosen to be investigated for its antioxidant, antimicrobial and anti-aging properties. The major component from pericarp of mangosteen, α-mangostin, was selected as the target compound in order to exploit new natural ingredients in developing safe and potent cosmetic products. Facial appearance is one of the important factors influencing social relations, thus it is important to evaluate the new potent antimicrobial active compound for the use in cosmetic products. Hence, dermatophyte and bacterial pathogen of skin are selected as the test organisms in antimicrobial study. *Garcinia mangostana* Linn. are known to possess a wide spectrum of pharmacologic properties, including antioxidant, anti-tumor, anti-allergic, anti-inflammatory, anti-bacterial, anti-fungal, and anti-viral activities (Shan et al., 2011). There has been no studies reported on anti-aging activities by α-mangostin of *Garcinia mangostana* Linn., thereby this investigation might be a significant approach to discover a new anti-aging active ingredients that can be utilized in the cosmetic industry.

1.3 The Objective of the Research

The aim of the research is to study the antioxidant, antimicrobial and anti-aging properties of α-mangostin from *Garcinia mangostana* Linn. pericarp extract.

1.4 The Scope of the Research

In order to achieve the objective, the scopes of the studies are identified as follow:-

i) DPPH (2, 2-diphenyl-1-picrylhydrazyl) radical scavenging activity and ABTS (2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid)) assay were carried out to measure the antioxidant activity of the α-mangostin.
ii) Broth microdilution test was done to screen the antimicrobial activity of α-mangostin against several selected bacteria and fungi strains.
iii) To study the anti-aging properties of α-mangostin, two assays were carried out. Anti-collagenase assay was performed to measure the anti-collagenase properties of α-mangostin.
iv) Collagen estimation assay was carried out to investigate the effect of α-mangostin on collagen synthesis *in vitro* by the fibroblast cells.

1.5 Significance of Study

The contributions of this study would be of interest in promoting the new trend that using wellness concept base on natural and plant materials in the skin care product formulation. Besides providing consumers with natural and plant base cosmetics and personal care products, these discoveries could found the concentration range able to apply to product development as cosmetic products. Moreover, the outcomes of the study could facilitate future application of mangosteen waste to be widely and synergistically used, at the same time preserving the environment.

REFERENCES

Abalaka, M. E. and Oyewole O. A. (2011). Antibacterial activities of *Asmina triloba* against some bacterial pathogens. *Journal of Microbiology Research*. 1 (1), 5-7.

Afaq, F., Zaid, M. A., Khan, N., Dreher, M., and Mukhtar, H. (2009). Protective effect of pomegranate-derived products on UVB-mediated damage in human reconstituted skin. *Experimental Dermatology*. 18(6), 553–561.

Aisha, A., Abu-Salah, K., Ismail, Z., Abdul, M.A. (2012). *In vitro* and *in vivo* anti-colon cancer effects of *Garcinia mangostana* xanthones extract. *BMC Complementary and Alternative Medicine.* 12, 104–112.

Alsterholm, M., Karami, N. and Faergemann, J. (2010). Antimicrobial activity of topical skin pharmaceuticals- An *In vitro* study. *Acta Dermato-Venereologica*. 90**,** 239-245.

Ahmad, M., Yamin, B. M., and Mat Lazim, A. (2013). A Study on Dispersion and Characterisation of a α- mangostin loaded pH Sensitive Microgel Systems. *Chemistry Central Journal*. 7, 85.

Al-Massarani, S. M., El-Gamal, A. A., Al-Musayeib, N. M., Mothana, R. A., Basudan, O. A., Al-Rehaily, A. J.,Farag, M., Assaf, M. H., El Tahir, K. H., and Maes, L. (2013). Phytochemical, Antimicrobial and Antiprotozoal Evaluation of *Garcinia Mangostana* Pericarp and α-mangostin, its Major Xanthone Derivative. *Molecules*. 18, 10599-10608.

Aly, R. (1991). Cutaneous microbiology. In Orkin, M., Maibach, H. I., Dahl, M. V. (Eds). *Dermatology*. (pp. 22-25). Los Altos: Appleton & Lange.

Aly, R. (1996). Microbial infections of skin and nails. In Baron, S. (Ed.) *Medical Microbiology*, *4th edition.* (Chapter 98). Galveston (TX): University of Texas Medical Branch.

Annan, K., Houghton, P. J. (2008). Antibacterial, antioxidant and fibroblast growth stimulation or aqueous extracts of *Ficus asperifolia* Miq. and *Gossypium arborerum* L., wound-healing plants of Ghana. *Journal of Ethnopharmacology*. 119, 141-144.

Arunrattiyakorn, P., Suksamrarn, S., Suwannasai, N., Kanzaki, H. (2011). Microbial metabolism of α-mangostin isolated from *Garcinia mangostana* L.. *Phytochemistry*. 72, 730–734.

Aslam, M. N., Lansky, E. P., and Varani, J. (2006). Pomegranate as a cosmeceutical source: Pomegranate fractions promote proliferation and procollagen synthesis and inhibit matrix metalloproteinases-1 production in human skin cells. *Journal of Ethnopharmacology*. 103, 311-318.

Aspé, E. and Fernández, K. (2011). The effect of different extraction techniques on extraction yield, total phenolic, and anti-radical capacity of extracts from *Pinus radiate* Bark. *Industrial Crops and Products*. 34, 838-844.

Awika, J. M., Rooney, L. W., Wu, X., Prior, R. L., CisnerosZevallos, L. (2003). Screening methods to measure antioxidant activity of sorghum (Sorghum bicolor) and sorghum products. *Journal of Agricultural Food and Chemistry*. 51, 6657-6662.

Beer, D., Joubert, E., Gelderblom, W. C. A. and Manley, M. (2002). Phenolic compounds: A review of their possible role as *in vivo* antioxidants of wine. *South African Journal of Enology and Viticulture*. 23(2), 48-65.

Behera, S., Manohar Babu, S. and Roja Ramani, Y. (2012). Phytochemical investigation and study on antioxidant properties of *Pongamia pinnata* hydro-alcoholic leaf extract. *Plant Sciences Feed.* 2(5), 74-78.

Benzie, I. F. F., and Strain, J. J. (1996). The ferric reducing ability of plasma (FRAP) as a measure of “Antioxidant Power”: The FRAP assay. *Analytical Biochemistry*. 239, 70-76.

Blokhina, O., Virolainen, E., Fagerstedt, K. V. (2003). Antioxidants, oxidative damage and oxygen deprivation stress: a review. *Annals of Botany*. 91, 179-194.

Booth, B. A., Polak, K. L., Uitto, J. (1980). Collagen biosynthesis by human skin fibroblasts. *Biochem Biophys Acta*. 607,145-160.

Brummer, Y. and Cui, S. W. (2005). Understanding Carbohydrate Analysis. In Cui, S. W. (Ed.) *Food Carbohydrates: Chemistry, Physical Properties, and Applications*. (pp 67-105). USA: Taylor & Francis Group.

Buelna-Chontal, M., Correa, F., Hernández-Reséndiz, S., Zazueta, C., Pedraza-Chaverri, J. (2011). Protective effect of α-mangostin on cardiac reperfusion damage by attenuation of oxidative stress. *Journal of Medicinal Food*. 14, 1370–1374.

Bullangpoti, V., Visetson, S., Milne, J., Milne, M., Sudthongkong, C., Pronbanlualap, S. (2007). Effects of alpha-mangostin from mangosteen pericarp extract and imidacloprid on Nilaparvata lugens (Stal.) and non-target organisms: toxicity and detoxification mechanism. *Communications in Agricultural and Applied Biological Science*. 72, 431–441.

Chae, H. S., Oh, S. R., Lee, H. K., Joo, S. H., Chin, Y. W. (2012). Mangosteen xanthones, α-and γ-mangostins, inhibit allergic mediators in bone marrow-derived mast cell. *Food Chemistry*. 134, 397–400.

Chairungsrilerd, N., Furukawa, K. I., Ohta, T., Nozoe, S., Ohizumi, Y. (1996). Pharmacological properties of α-mangostin, a novel histamine H1 receptor antagonist. *European Journal of Pharmacology*. 314, 351–356.

Chakraborty, P., Kumar, S., Dutta, D. and Gupta, V. (2009). Role of antioxidants in common health diseases. *Research Journal of Pharmacy and Technology*. 2(2), 238-244.

Chan, M. M. Y. (2002). Antimicrobial effect of resveratrol on dermatophytes and bacterial pathogens of the skin. *Biochemical Pharmacology*. 63, 99-104.

Chanvorachote, P., Pongrakhananon, V., Luanpitpong, S., Chanvorachote, B., Wannachaitasit, S., and Nimmannit, U. (2009). Type I pro-collagen promoting and anti-collagenase activities of *Phyllanthus emblica* extract in mouse fibroblasts. *Journal of Cosmetic Science*. 60, 395-403.

Chen, L. G., Yang, L. L., Wang, C. C. (2008). Anti-inflammatory activity of mangostins from *Garcinia mangostana*. *Food and Chemical Toxicology*. 46, 688–693.

Chermahini, S. H., Majid, F. A. A., Sarmidi, M. R. (2011). Cosmeceutical value of herbal extracts as natural ingredients and novel technologies in anti-aging. *Journal of Medicinal Plants Research*. 5(14), 3074-3077.

Chin, Y.-W., Kinghorn, A.D. (2008). Structural characterization, biological effects, and synthetic studies on xanthones from mangosteen (*Garcinia mangostana*), a popular botanical dietary supplement. *Mini-Reviews in Organic Chemistry*. 5, 355–364.

Cho, S., Won, C. H., Lee, D. H., Lee, M. J., Lee, S., So, S. H., Lee, S. K., Koo, B. S., Kim, N. M., Chung, J. H. (2009). Red ginseng root extract mixed with *Torilus fructus* and Cornifructus improves facial wrinkles and increases type I procollagen synthesis in human skin: a randomized, double-blind, placebo-controlled study. *Journal of Medicinal Food*. 12, 1252–1259.

Choi, H. K., Kim, D. H., Kim, J. W., Ngadiran, S., Sarmidi, M. R., and Park, C. S. (2010). *Labisia pumila* extract protects skin cells from photoaging caused by UVB irradiation. *Journal of Bioscience and Bioengineering*. 109(3), 291–296.

Chomnawang, M. T., Sakagami, S. S., Nukoolkarn, V. S., Gritsanapan, W. (2005). Antimicrobial effects of Thai medicinal plants against acne-inducing bacteria. *Journal of Ethnopharmacology*. 101, 330–333.

Chomnawang, M. T., Surassmo, S., Nukoolkarn, V. S., Gritsanapan, W. (2007). Effect of Garcinia mangostana on inflammation caused by *Propionibacterium acnes*. *Fitoterapia*. 78, 401–408.

Chu, D. H. (2008). Overview of biology, development, and structure of skin. In K. Wolff, L. A., Goldsmith, S. I., Katz, B. A., Gilchrest, A. S., Paller, & D. J. Leffell (Eds.). *Fitzpatrick's dermatology in general medicine* (7th ed., pp 57-73). New York: McGraw-Hill.

Cruse, J. M. and Lewis, R. E. (2010). *Atlas of Immunology*. (3rd ed). USA: CRC Press.

Cui, J., Hu, W., Cai, Z., Liu, Y., Li, S., Tao, W., Xiang, H. (2010). New medicinal properties of mangostins: analgesic activity and pharmacological characterization of active ingredients from the fruit hull of (*Garcinia mangostana* L.). *Pharmacology Biochemistry and Behavior*. 95, 166–172.

Curtis, C. (1998). Use and abuse of topical dermatological therapy in dogs and cats. Part 1. Shampoo. *In Practice*. 20, 244-251

Deng, J., Cheng, W. Y. and Yang, G. Z. (2011). A novel antioxidant activity index (AAU) for natural products using the DPPH assay. *Food Chemistry*. 125, 1430-1435.

Deschamps, J. D., Gautschi, J. T., Whitman, S., Johnson, T. A., Gassner, N. C., Crews, P., Holman, T. R. (2007). Discovery of platelet-type 12-human lipoxygenase selective inhibitors by high throughput screening of structurally diverse libraries. *Bioorganic & Medicinal Chemistry*. 15, 6900–6908.

Devi Sampath, P., Vijayaraghavan, K. (2007). Cardioprotective effect of α-mangostin, a xanthone derivative from mangosteen on tissue defense system against isoproterenol-induced myocardial infarction in rats. *Journal of Biochemical and Molecular Toxicology*. 21, 336–339.

Devi, W. R., Singh, S. B. and Singh, C. B. (2013). Antioxidant and anti-dermatophytic properties leaf and stem bark of *Xylosma longifolium* clos. *BMC Complementary & Alternative Medicine*. 13, 155.

Dragendorff, O. (1930). Über das Harz von Garcinia Mangostana L. *Liebigs Annalen der Chemie*. 482, 280–301.

Dupont, E., Gomez, J., Léveillé, C., Bilodeau, D. (2010). From hydration to cell turnover: An integral approach to antiaging. *Cosmetics & Toiletries*. 125(3), 1-9.

Fan, C. T., Su, J. D. (1997). Antioxidative mechanism of isolated components from methanol extract of fruit hulls of *Garcinia Mangostana* L. *Journal of the Chinese Chemical Society*. 35, 540–551.

Farooqi, A. H. A., Sharma, S., and Kumar, S. (2002). Herbal skin care formulation and a process for the preparation thereof. US Patent 6368639. http://patent.ipexl.com/US/6368639.html

Feingold, D. S. (1986). Bacterial adherence, colonization, and pathogenicity. *Archives of Dermatology*. 122, 161-163.

Fibrocell Science. (2012). Your Skin. Retrieved from the My Laviv website: http://mylaviv.com/your-skin/

Fisher, G. J., Kang, S., Varani, J., Bata-Csorgo, Z., Wan, Y., Datta, S., Voorhees, J. J. (2002). Mechanisms of photoaging and chronological skin aging. *Archives of Dermatology*. 138(11), 1462-1470.

Fisher, G. J., Varani, J. and Voorhees, J. J. (2008). Looking older: Fibroblast collapse and therapeutic implications. *Archives of Dermatology*. 144(5), 666-672.

Fisher, G. J., Quan, T. H., Purohit, T., Shao, Y., Cho, M. K., He, T. Y., Varani, J., Kang, S. W., and Voorhees, J. J. (2009). Collagen fragmentation promotes oxidative stress and elevates Matrix Metalloproteinase-1 in fibroblasts in aged human skin. *The American Journal of Pathology*. 174(1), 101-114.

Fujii, T., Wakaizumi, M., Ikami, T., Saito, M. (2008). Amla (*Emblica officinalis* Gaertn.) extract promotes procollagen production and inhibits matrix metalloproteinase-1 in human skin fibroblasts. *Journal of Ethnopharmacology*. 119(1), 53-57.

Fusco, D., Colloca, G., Monaco, M. R. L. and Cesari, M. (2007). Effects of antioxidant supplementation on the aging process. *Clinical Interventions in Aging*. 2(3), 377-387.

Ganceviciene, R., Liakou, A. I., Theodoridis, A., Makrantonaki, E., and Zouboulis, C. C. (2012). Skin anti-aging strategies. *Archive of Dermato-endocrinology*. 4 (3), 308-319.

Geetha, R. V., Roy, A., and Lakshimi, T. (2011). Evaluation of anti-bacterial activity of fruit rind extract of *Garcinia Mangostana* Linn on enteric pathogens- An in vitro study. Asian *Journal of Pharmaceutical and Clinical Research*. 4(2), 115-118.

Ginsburg, H. and Deharo, E. (2011). A call for using natural compounds in the development of new antimalarial treatments-an introduction. *Malaria Journal*. 10, 1-50.

Gopalakrishnan, C., Shankaranarayanan, D., Kameswaran, L., Nazimudeen, S. (1980). Effect of mangostin, a xanthone from *Garcinia mangostana* Linn. in immunopathological & Inflammatory reactions. *Indian Journal of Experimental Biology*. 18, 843–846.

Gopalakrishnan, G., Banumathi, B., Suresh, G. (1997). Evaluation of the antifungal activity of natural xanthones from *Garcinia mangostana* and their synthetic derivatives. *Journal of Natural Products*. 60, 519–524.

Govindachari, T. R. K. P., Muthukumaraswamy, N. (1971). Xanthones of Garcinia Mangostana Linn. *Tetrahedron*. 27, 3919–3926.

Haftek, M., Mac, M. S., LeBitoux, M. A., Creidi, P., Seite, S., Rougier, A., Humbert, P. (2008). Clinical, biometric and structural evaluation of the long-term effects of a topical treatment with ascorbic acid and madecassoside in photoaged human skin. *Experimental Dermatology*. 17, 946–952.

Hani, A. F. M. and Fitriyah, H. (2014). Skin Lesion Thickness Assessment. In Hani, A. F. M. (Ed.) *Surface Imaging for Biomedical Applications.* New York: CRC Press.

Harman D. (1957). Aging: a theory based on free radical and radiation chemistry. *The Journal of Gerontology*. 2, 298–300.

Haruenkit, R.., Poovarodom, S., Leontowicz, H., Leontowicz, M., Sajewicz, M., Kowalska, T., Delgado, E., Rocha, N. E., Gallegos, J. A., Trakhtenberg, S., Gorinstein, S. (2007). Comparative study of health properties and nutritional value of durian, mangosteen and snake fruit: Experiments in vitro and in vivo. *Journal of Agricultural and Food Chemistry*. 55, 5842–5849.

Hasham, R., Choi, H. K., Park, C.S. (2014). *Ficus deltoidea* Extract Protects HaCaT Keratinocytes from UVB Irradiation-Induced Inflammation. *International Journal of Biological, Veterinary, Agricultural and Food Engineering*. 8 (11), 1096-1100.

Hay, R., Bendeck, S. E., Chen, S., Estrada, R., Haddix, A., McLeod, T., Mahé, A. (2006). Disease Control Priorities in Developing Countries, 2nd edition. In Jamison, D. T., Breman, J.G., Measham, A. R., Alleyne, G., Claeson, M., Evans, D. B., Jha, P., Mills, A., Musgrove, P. (Ed.) *Chapter 37: Skin Diseases.* (pp 707-721). Washington: The World Bank Group.

Hayes, A. J., Markovic, B. (2002). Toxicity of Australian essential oil Backhousia citriodora (Lemon myrtle). Part 1. Antimicrobial activity and in vitro cytotoxicity. *Food and Chemical Toxicology.* 40, 535–543.

Huang, D., Ou, B., Prior, R. L. (2005). The chemistry behind antioxidant capacity assays. *Journal of Agricultural Food and Chemistry*. 53, 1841-1856.

Hung, S. H., Shen, K. H., Wu, C. H., Liu, C. L., Shih, Y. W. (2009). α-Mangostin suppresses PC-3 human prostate carcinoma cell metastasis by inhibiting matrix metalloproteinase-2/9 and urokinase-plasminogen expression through the JNK signaling pathway. *Journal of Agricultural and Food Chemistry*. 57, 1291–1298.

Iinuma, M., Tosa, H., Tanaka, T., Asai, F., Kobayashl, Y., Shimano, R., Miyauchi, K. I. (1996). Antibacterial activity of xanthones from guttiferaeous plants against methicillin-resistant *Staphylococcus aureus*. *Journal of Pharmacy and Pharmacology*. 48, 861–865.

Inomata, S., Matsunaga, Y., Amano, S., Takada, K., Kobayashi, K., Tsunenaga, M., Nishiyama, T., Kohno, Y., Fukuda, M. (2003). Possible involvement of gelatinases in basement membrane damage and wrinkle formation in chronically ultraviolet B-exposed hairless mouse. *Journal of Investigative Dermatology*. 120(1), 128–134.

Itoh, T., Ohguchi, K., Iinuma, M., Nozawa, Y., Akao, Y. (2008). Inhibitory effect of xanthones isolated from the pericarp of *Garcinia mangostana* L. on rat basophilic leukemia RBL-2H3 cell degranulation. *Bioorganic & Medicinal Chemistry*. 16, 4500–4508.

James, W. D., Berger, T. G., & Elston, D. M. (2006). *Andrews' diseases of the skin: Clinical dermatology* (10th ed.). Philadelphia: Elsevier Saunders.

Janeway, C. A., Jr, Travers, P., Walport, M., and Shlomchik, M. J. (2001). *Immunobiology: The Immune System in Health and Disease.* (5th ed). New York: Garland Science.

Jiang, D. J., Dai, Z., Li, Y. J. (2004). Pharmacological effects of xanthones as cardiovascular protective agents. *Cardiovascular Drug Review*. 22, 91–102.

Jo, W. S., Yang, K. M., Park, H. S., Kim, G. Y., Nam, B. H., Jeong, M. H., and Choi, Y. J. (2012). Effect of Mircoalgal Extracts of Tetraselmis suecica against UVB-induced Photoaging in Human Skin Fibroblasts. *Toxicological Research*. 28(4), 241-248.

Jung, H. A., Su, B. N., Keller, W. J., Mehta, R. G., and Kinghorn, A. D. (2006). Antioxidant Xanthones from the Pericarp of *Garcinia mangostana* (Mangosteen). *Journal of Agricultural and Food Chemistry*. 54(6), 2077-2082.

Jung, E., Lee, J., Baek, J., Jung, K., Lee, J., Huh, S., Kim, S., Koh, J., Park, D. (2007). Effect of *Camellia Japonica* oil on human type I procollagen production and skin barrier function. *Journal of Ethnopharmacology*. 112, 127–131.

Jung, H. Y., Shin, J. C., Park, S. M., Kim, N. R., Kwak, W. J., Choi, B. H. (2014). *Pinus densiflora* extract protects human skin fibroblasts against UVB-induced photoaging by inhibiting the expression of MMPs and increasing type I procollagen expression. *Toxicology Reports I*. 658-666.

Kanitakis, J. (2002). Anatomy, histology and immunohistochemistry or normal human skin. *European Journal of Dermatology*. 12(4), 390-401.

Kang, S., Fisher, G. J., Voorhees, J. J. (2001). Photoaging: pathogenesis, prevention, and treatment. *Clinics in Geriatric Medicine*. 17, 643-659.

Kaomongkolgit, R., Chaisomboon, N., and Pavasant, P. (2011). Apoptotic effect of alpha-mangostin on head and neck squamous carcinoma cells. *Archives of Oral Biology*. 56, 483-490.

Kaomongkolgit, R., Jamdee, K., Chaisomboon, N. (2009). Antifungal activity of alpha-mangostin against *Candida albicans*. *Journal of Oral Science*. 51, 401–406.

Kasote, D. M., Ktyare, S. S., Hegde, M. V., Bae, H. H. (2015). Significance of Antioxidant Potential of Plants and its Relevance to Therapeutic Applications. *International Journal of Biological Sciences*. 11(8), 982-991.

Keiser, J., Vargas, M., Winter, R. (2012). Anthelminthic properties of mangostin and mangostin diacetate. *Parasitology International*. 61, 369–371.

Kim, S., Chung, J. H., (2008a). Berberine prevents UV-induced MMP-1 and reduction of type I procollagen expression in human dermal fibroblasts. *Phytomedicine*. 15, 749–753.

Kim, S., Kim, Y., Kim, J. E., Cho, K. H., Chung, J. H., (2008b). Berberine inhibits TPA-induced MMP-9 and IL-6 expression in normal human keratinocytes. *Phytomedicine*. 15, 340–347.

Kim, S. Y., Go, K. C., Song, Y. S., Jeong, Y. S., Kim, E. J., Kim, B. J. (2014a). Extract of the mycelium of *T. matsutake* inhibits elastase activity and TPA-induced MMP-1 expression in human fibroblasts. *International Journal of Molecular Medicine*. 34(6), 1613-1621.

Kim, S. Y., Kim, J. E., Bu, H. J., Hyun, C. G., Lee, N. H. (2014b). Chemical constituents of *Tilia taquetii* leaves and their inhibition of MMP-1 expression and elastase activities. *Natural Product Communication*. 9(12), 1683-1685.

Kiviluoma, L. (2013). *Vital Face: Facial Exercises and Massage for Health and Beauty*. USA: Singing Dragon.

Koh, J. J., Qiu, S. X., Zou, H. X., Lakshminarayanan, R., Li, J. G., Zhou, X. J., Tang, C., Saraswathi, P., Verma, C., Tan, D. T. H., Tan, A. L., Liu, S. P., Beuerman, R. W. (2013). Rapid bactericidal action of alpha-mangostin against MRSA as an outcome of membrane targeting. *Biochimica et Biophysica Acta*. 1828, 834-844.

Kohen, R. and Nyska, A. (2002). Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods for their quantification. *Toxicologic Pathology*. 30(6), 620-650.

Krajarng, A., Nilwarankoon, S., Suksamrarn, S., Watanapokasin, R. (2012). Antiproliferative effect of α-mangostin on canine osteosarcoma cells. *Research in Veterinary Science*. 93, 788–794.

Kumari, S., and Khurana, S. M. P. (2013). Cosmeceuticals: current trends and market preparations. *IOSR Journal of Pharmacy and Biological Sciences*. 8(3), 45-48.

Kurz, S. W. and Monte, T. (2006). *Awakening Beauty: The Dr. Hauschka Way*. USA: Clairview Books.

Larson, R. A. (1988). The antioxidants of higher plants. *Phytochemistry*. 27(4), 969-978.

Larson, R. T., Lorch, J. M., Pridgeon, J. W., Becnel, J. J., Clark, G. G., Lan, Q. (2010). The biological activity of alpha-mangostin, a larvicidal botanic mosquito sterol carrier protein-2 inhibitor. *Journal of Medical Entomology*. 47, 249–257.

Laura Wood (2014, May 20). Research and Markets: Global Cosmeceuticals Market Outlook 2018-Forecasts & Opportunities for the US $35 Billion Industry. *Business Wire*. Retrieved Oct 22, 2014, from http://www.businesswire.com/news/home/20140520006627/en/Research-Markets-Global-Cosmeceuticals-Market-Outlook-2018#.VERz7Iano5d

Lee, J., Jung, E., Kim, Y., Park, J., Park, J., Hong, S., Kim, J., Hyun, C., Kim, Y. S., Park, D. (2006). Asiaticoside induces human collagen I synthesis through TGF_receptor I kinase (T_RI kinase)-independent Smad signaling. *Planta Medica*. 72, 324–328.

Lee, H. J., Kim, J. S., Song, M. S., Seo, H. S., Moon, C., Kim, J. C., Jo, S. K., Jang, J. S., Kim, S. H. (2009a). Photoprotective effect of red ginseng against UV radiation-induced chronic skin damage in the hairless mouse. *Phytotherapy Research*. 23, 399–403.

Lee, Y. B., Ko, K. C., Shi, M. D., Liao, Y. C., Chiang, T. A., Wu, P. F., Shih, Y. X., Shih, Y. W. (2010). α-Mangostin, a novel dietary xanthone, suppresses TPA-mediated MMP-2 and MMP-9 expressions through the ERK signaling pathway in MCF-7 human breast adenocarcinoma cells. *Journal of Food Science*. 75, H13–H23.

Lee, Y. L., Lee, M. H., Chang, H. J., Huang, P. Y., Huang, I. J., Cheng, K. T., Leu, S. J. (2009). Taiwanese Native Plants Inhibit Matrix Metalloproteinase-9 Activity after Ultraviolet B Irradiation. *Molecules*. 14, 1062-1071.

Leu, S. J., Lin, Y. P., Lin, R. D., Wen, C. L., Cheng, K. T., Hsu, F. L., and Lee, M. H. (2006). Phenolic Constituents of *Malus doumeri* var. *formosana* in the Field of Skin Care. *Biological and Pharmaceutical Bulletin.* 29(4), 740-745.

Lemanska, K., Szymusiak, H., Tyrakowska, B., Zielinski, R., Soffer, A. E. M. F., Rietjens, I. M. C. M. (2001). The influence of pH on the antioxidant properties and the mechanisms of antioxidant action of hydroxyflavones. *Free Radical Biology & Medicine*. 31, 869-881.

Leong, L., Shui, G. (2002). An investigation of antioxidant capacity of fruits in Singapore markets. *Food Chemistry*. 76, 69–75.

Lobo, V., Patil, A., Phatak, A. and Chandra, N. (2010). Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacognosy Review*. 4(8), 118-126.

Losio, N., Bertasi, B., D'Abrosca, F., Ferrari, M., Avalle, N., and Fishbach, M. (1999). In Vitro Product Safety Evaluation: A screening Study on a series of Finished Cosmetic Products. *Alternatives to Laboratory Animals*. 27, 351.

Mahabusarakam, W., Proudfoot, J., Taylor, W., Croft, K. (2000). Inhibition of lipoprotein oxidation by prenylated xanthones derived from mangostin. *Free Radical Research*. 33, 643-659.

Martinez, A., Galano, A., and Vargas, R. (2011). Free Radical Scavenger Properties of α-mangostin: Thermodynamics and Kinetics of HAT and RAF Mechanisms. *The Journal of Physical Chemistry*. 115(43), 12591-12598.

Matsumoto, K., Akao, Y., Kobayashi, E., Ohguchi, K., Ito, T., Tanaka, T., Iinuma, M., Nozawa, Y. (2003). Induction of apoptosis by xanthones from mangosteen in human leukemia cell lines. *Journal of Natural Products*. 66, 1124–1127.

Matsumoto, K., Akao, Y., Ohguchi, K., Ito, T., Tanaka, T., Iinuma, M., Nozawa, Y. (2005). Xanthones induce cell-cycle arrest and apoptosis in human colon cancer DLD-1 cells. *Bioorganic & Medicinal Chemistry*. 13, 6064–6069.

McConell, K. W., Kirby, J. P. and Mazuski, J. E. (2012). Cellulitis/ Fasciitis/ Myositis. In Kollef, M. and Isakow, W. (Ed.) *The Washington Manual of Critical Care, 2nd edition.* USA: Lippincott Williams & Wilkins, a Wolters Kluwer business.

Mescher, A. L. (2009). *Junqueira's Basic Histology: Text & Atlas.* United States: McGraw Hill Professional.

Mishra, K. Ojha, H. and Chaudhury, N. K. (2012). Estimation of antiradical properties of antioxidants using DPPH assay: A critical review and results. *Food Chemistry*. 130, 1036-1043.

Mohamed, M. A. A., Jung, M., Lee, S. M., Lee, T. H., Kim, J. Y. (2014). Protective effect of *Disporum sessile* D. Don extract against UVB-induced photoaging via suppressing MMP-1 expression and collagen degradation in human skin cells. *Journal of Photochemistry and Photobiology B: Biology*. 133, 73-79.

Moon, H., Jung, J. C. (2006). Effect of meso-dihydroguaiaretic acid from *Machilus thunbergii* Sieb and Zucc on MMP-1 expression in heat shock-induced cultured primary human fibroblasts. *Phytotherapy Research*. 20, 714–716.

Morganti, P. (2012). Skin Photoprotection and nutraceuticals: an overview. In Preedy, V. R. (Ed.) *Handbook of Diet, Nutrition and the Skin*. The Netherlands: Wageningen Academic Publishers.

Morton, J. (1987). *Fruits of warm climates*. USA: Creative Resource Systems Inc. Page 301-304.

Mukherjee, P. K., Leidich, S. D., Isham, N., Leitner, I., Ryder, N. S., and Ghannoum, M. A. (2003). Clinical Trichophyton rubrum strain exhibiting primary resistance to terbinafine. *Antimicrobial Agents and Chemotherapy*. 47, 82–86.

Mukherjee, S., Date, A., Patravale, V., Korting, H. C., Roeder, A., Weindl, G. (2006). Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety. *Clinical Interventions in Aging.* 1(4), 327-348.

Murkherjee, P. K., Maity, N., Nema, N. K., Sarkar, B. K. (2011). Bioactive compounds from natural resources against skin aging. *Phytomedicine.* 19, 64-73.

Murina, A. T., Kerisit, K. G., Boh, E. E. (2012). Mechanisms of skin aging. *Cosmetic Dermatology*. 25(9), 399-402.

Nabandith, V., Suzui, M., Morioka, T., Kaneshiro, T., Kinjo, T., Matsumoto, K., Akao, Y., Iinuma, M., Yoshimi, N. (2004). Inhibitory effects of crude alpha-mangostin, a xanthone derivative, on two different categories of colon preneoplastic lesions induced by 1, 2-dimethylhydrazine in the rat. *Asian Pacific Journal of Cancer Prevention*. 5, 433–438.

Naczk, M. and Shahidi, F. (2004). Extraction and analysis of phenolics in food. *Journal of chromatography A.* 1054(1-2), 95-111.

Nakagawa, Y., Iinuma, M., Naoe, T., Nozawa, Y., Akao, Y. (2007). Characterized mechanism of α-mangostin-induced cell death: Caspase-independent apoptosis with release of endonuclease-G from mitochondria and increased miR-143 expression in human colorectal cancer DLD-1 cells. *Bioorganic & Medicinal Chemistry*. 15, 5620–5628.

National Committee for Clinical Laboratory Standards. (1998). Reference method for broth dilution antifungal susceptibility testing of conidium-forming filamentous fungi. Proposed standard, M38-P. Wayne, PA: National Committee for Clinical Laboratory Standards.

National Committee for Clinical Laboratory Standards. (2000). Methods for dilution antimicrobials susceptibility tests for bacteria that grow aerobically. Approved standard, M7-A5. Wayne, PA: National Committee for Clinical Laboratory Standards.

Negi, P. S. (2012). Plant extracts for the control of bacterial growth: Efficacy, stability and safety for food application. *International Journal of Food Microbiology*. 156, 7-17.

Negi, J. S., Bisht, V. K., Singh, P., Rawat, M. S. M. and Joshi, G. P. (2013). Naturally Occurring Xanthones: Chemistry and Biology. *Journal of Applied Chemistry.* 2013, 1-9.

Noctor, G. and Foyer, C. H. (1998). Ascorbate and glutathione: keeping active oxygen under control. *Annual Review of Plant Physiology and Plant Molecular Biology*. 49, 249-279.

Nohynek, G. J., Antignac, E., Re, T., Toutain, H. (2009). Safety Assessment of personal care products/cosmetics and their ingredients. *Toxicology and Applied Pharmacology*. 243(2), 239-259.

Nordberg, J. and Arner, E. S. J. (2001). Reactive oxygen species, antioxidants, and the mammalian thioredoxin system. *Free Radical Biology & Medicine*. 31(11), 1287-1312.

Obolskiy, D., Pischel, I., Siriwatanamentanon, N., Heinrich, M. (2009). *Garcinia mangostana* L.: a phytochemical and pharmacological review. *Phytotherapy Research.* 23 (8), 1047-1065.

Oh, H. I., Shim, J. S., Gwon, S. H., Kwon, H. J., Hwang, J. K. (2009). The effect of xanthorrhizol on the expression of matrix metalloproteinase-1 and type-I procollagen in ultraviolet-irradiated human skin fibroblasts. *Phytotherapy Research*. 23, 1299–1302.

Ozsoy, N., Can, A., Yanardag, R. and Akev, N. (2008). Antioxidant activity of *Smilax excelsa* L. leaf extracts. *Food Chemistry*. 110(3), 571-583.

Palmer, D. M. and Kitchin, J. S. (2010). Oxidative damage, skin aging, antioxidants and a novel antioxidant rating system. *Journal of Drugs In Dermatology*. 9(1), 11-15.

Paradisi, M., McClintock, D., Boguslavsky, R. L., Pedicelli, C., Worman, H. J and Djabali, K. (2005). Dermal fibroblast in hutchinson-gilford progeria syndrome with the Lamin A G608G mutation have dysmorphic nuclei and are hypersensitive to heat stress. *Cell Biology*. 6, 27.

Pedraza-Chaverri, J., Cárdenas-Rodríguez, N., Orozco-Ibarra, M., Pérez-Rojas, J. M. (2008). Medicinal properties of mangosteen (Garcinia Mangostanan). *Food and Chemical Toxicology*. 46, 3227-3239.

Pedraza-Chaveri, J., Reyes-Fermin, L. M., Nolasco-Amaya, E. G., Orozco-Ibarra, M., Medina-Campos, O. N., Gonzalez-Cuahutencos, O., Rivero-Cruz, I., and Mata, R. (2009). ROS Scavenging Activity and Neuroprotective Effect of α-Mangostin against 3-Nitropropionic Acid in Cerebellar Granule Neurons. *Experimental and Toxicologic Pathology*. 61, 491-501.

Peres, V., Nagem, T. J., Faustino de Oliveira, F. (2000). Tetraoxygenated naturally occurring xanthones. *Phytochemistry*. 55, 683–710.

Pérez-Rojas, J. M., Cruz, C., García-López, P., Sánchez-González, D. J., Martínez-Martínez, C. M., Ceballos, G., Espinosa, M., Meléndez-Zajgla, J., Pedraza-Chaverri, J. (2009). Renoprotection by α-mangostin is related to the attenuation in renal oxidative nitrosative stress induced by cisplatin nephrotoxicity. *Free Radical Research*. 43, 1122–1132.

Pothitirat, W., and Gritsanapan, W. (2008). Quantitative Analysis of Total Mangostin in *Garcinia Mangostana* Fruit Rind. *Journal of Health Research*. 22(4), 161-166.

Pothitirat, W. and Gritsanapan, W. (2009). HPLC Quantitative Analysis Method for the Determination of α- mangostin in Mangosteen Fruit Rind Extract. *Thai Journal of Agricultural Science*. 42(1), 7-12.

Prasad, K. N. (2011). *Micronutrients in Health and Disease*. CRC Press: United States of America.

Price, P. and Frey, K. B. (2003). *Microbiology for Surgical Technologists.* USA: Delmar Learning.

Prior, R. L., Wu, X. L. and Schaich, K. (2005). Standardized Methods for the Determination of Antioxidant Capacity and Phenolics in Foods and Dietary Supplements. *Journal of Agricultural Food and Chemistry*. 53, 4290-4302.

Puripattanavong, J. K. W., Khajorndetkun, W., Chansathirapanich, W. (2006). Improved isolation of α-mangostin from the fruit hull of Garcinia mangostana and its antioxidant and antifungal activity. *Planta Medica*. 72, 1078.

Quan, X., Wang, Y., Liang, Y., Tian, W., Ma, Q., Jiang, H., Zhao, Y. (2012). α-Mangostin induces apoptosis and suppresses differentiation of 3T3–L1 cells via inhibiting fatty acid synthase. *PLoS One*. 7, 33376–33379.

Rawani, A., Pal, S. and Chandra, G. (2011). Evaluation of antimicrobial properties of four plant extracts against human pathogens. *Asian Pacific Journal of Tropical Biomedicine.* 1(1), S71-S75.

Re, R., Pellegrinin, N., Proteggente A., Pannala, A., Yang, M., Rice-Evans, C. (1999). Antioxidant activity applying an improved ABTS radical cation decolorization assay. *Free Radical Biology and Medicine*. 26, 1231-1237.

Rice-Evans, C. A., Miller, J. M., and Paganga, H. (1996). Structure-antioxidant activity relationship of flavonoids and phenolic acids. *Free Radical Biology & Medicine*. 20, 933-956.

Riss, T. L., Moravec, R. A., Niles, A. L., Benink, H. A., Worzella, T. J., Minor, L. (2013). Cell Viability Assays. In Sittampalam, G. S., Coussens, N. P., Nelson, H., Arkin, M., Auld, D., Austin, C., Bejcek, B., Glicksman, M., Inglese, J., Iversen, P. W., Li, Z. Y., McGee, J., McManus, O., Minor, L., Napper, A., Peltier, J. M., Riss, T., Trask, J., Weidner, J. (Eds.) Assay Guidance Manual [Internet]. Bethesda (MD): Eli Lilly & Company and the National Center for Advancing Translational Sciences.

Rivero-Pérez, M. D., Muñiz, P., Gonzalez-Sanjosé, M. L. (2007). Antioxidant profile of red wines evaluated by total antioxidant capacity, scavenger activity, and biomarkers of oxidative stress methodologies. *Journal of Agricultural and Food Chemistry*. 55(14), 5476-5483.

Rodriguez, M. (2015). *Microbiology for Surgical Technologists, Second Edition.* USA: Cengage Learning.

Roy, A., Sahu, R. K., Matlam, M., Deshmukh, V. K., Dwivedi, J., and Jha, A. K. (2013). *In vitro* techniques to assess the proficiency of skin care cosmetic formulations. *Pharmacognosy Review*. 7(14), 97-106.

Ryoo, I. J., Moon, E. Y., Kim, Y. H., Lee, I. S., Choo, S. J., Bae, K. H., Yoo, I. D. (2010). Anti-Skin Aging Effect of Syriacusins from *Hibiscus Syriacus* on Ultraviolet-Irradiated Human Dermal Fibroblast Cells. *Biomolecules & Therapeutics*. 18 (3), 300-307.

Sakagami, Y., Iinuma, M., Piyasena, K., Dharmaratne, H. (2005). Antibacterial activity of α-mangostin against vancomycin resistant Enterococci (VRE) and synergism with antibiotics. *Phytomedicine*.12, 203–208.

Saltzman, W. M. (2004). *Tissue engineering: Principles for the design of replacement organ and tissues.* New York: Oxford University Press.

Sánchez-Pérez, Y., Morales-Bárcenas, R., García-Cuellar, C.M., López-Marure, R., Calderon-Oliver, M., Pedraza-Chaverri, J., Chirino, Y.I. (2010). The α-mangostin prevention on cisplatininduced apoptotic death in LLC-PK1 cells is associated to an inhibition of ROS production and p53 induction. *Chemico-Biological Interactions.* 188, 144–150.

Sarma, A. D., Mallick, A. R. and Ghosh, A. K. (2010). Free Radicals and Their Role in Different Clinical Conditions: An Overview. *International Journal of Pharma Sciences and Research*. 1(3), 185-192.

Sasidharan, S., Chen, Y., Saravanan, D., Sundram, K. M., and Yoga Latha, L. (2011). Extraction, Isolation and Characterization of Bioactive Compounds from Plant Extracts. *African Journal Traditional Complementary Alternative Medicine*. 8(1), 1-10.

Satong-aun, W., Assawarachan, R., and Noomhorm, A. (2011). The Influence of Drying Temperature and Extraction Methods on α-mangostin in Mangosteen Pericarp. *Journal of Food Science and Engineering*. 1, 85-92.

Schade, J. (2006). *The Complete Encyclopedia of Medicine and Health*. USA: Foreign Media Books.

Scheibmeir, H. D., Christensen, K., Whitaker, S. H., Jegaethesan, J., Clancy, R. and Pierce, J. D. (2005). A review of free radicals and antioxidants for critical care nurses. *Intensive and Critical Care Nursing*. 21(1), 24-28.

Schmid, W. (1855). Ueber das mangostin. *Liebigs Annalen der Chemie*. 93, 83–89.

Seo, Y. K., Jung, S. H., Song, K. Y., Park, J. K., Park, C. S. (2010). Anti-photoaging effect of fermented rice bran extract on UV-induced normal skin fibroblasts. *European Food Research and Technology*. 231(2), 163-169.

Shahidi, F. and Wanasundara, P. K. J. P .D. (1992). Phenolic antioxidants. *Critical reviews in food science and nutrition*. 32(1), 67-103.

Shan, T., Ma, Q., Guo, K., Liu, J., Li, W., Wang F., and Wu, E. (2011). Xanthones from Mangosteen Extracts as Natural Chemopreventive Agents: Potential Anticancer Drugs. *Current Molecular Medicine*. 11(8), 666-677.

Shan, Y., and Zhang, W. (2010). Preparative Separation of Major Xanthones from Mangosteen Pericarp using High Performance Centrifugal Partition Chromatography. *Journal of Separation Science*. 33, 1274-1278.

Shankaranarayan, D., Gopalakrishnan, C., Kameswaran, L. (1979). Pharmacological profile of mangostin and its derivatives. *Archives Internationales de Pharmacodynamie et de thérapie*. 239, 257–269.

Shibata, M. A., Iinuma, M., Morimoto, J., Kurose, H., Akamatsu, K., Okuno, Y., Akao, Y., Otsuki, Y. (2011). α-Mangostin extracted from the pericarp of the mangosteen (*Garcinia mangostana* Linn) reduces tumor growth and lymph node metastasis in an immunocompetent xenograft model of metastatic mammary cancer carrying a p53 mutation. *BMC Medicine*. 9, 69–76.

Shih, Y. W., Chien, S. T., Chen, P. S., Lee, J. H., Wu, S. H., Yin, L. T. (2010). Alpha-mangostin suppresses phorbol 12-myristate 13-acetateinduced MMP-2/MMP-9 expressions via avb3 integrin/FAK/ERK and NF-jB signaling pathway in human lung adenocarcinoma A549 cells. *Cell Biochemistry and Biophysics*. 58, 31–44.

Shim, J. S., Choi, E. J., Lee, C. W., Kim, H. S., Hwang, J. K. (2009). Matrix metalloproteinase-1 inhibitory activity of *Kaempferia pandurata* Roxb. *Journal of medicinal food*. 12(3), 601-607.

Shrivastava, H. Y., Ravikumar, T., Shanmugasundaram, N., Babu, M. and Nair, B. U. (2005). Cytotoxicity studies of chromium (III) complexes on human dermal fibroblasts. *Free Radical Biology and Medicine*. 38(1), 58-69.

Sjerobabski-Masnec, I. and Šitum, M. (2010). Skin Aging. *Acta Clinica Croatica*. 49, 515-519.

Souza, M. E., Pinto, M. M. M. (2005). Síntesis of xanthones: an overview. *Free Radical Research*. 12, 2447–2479.

Suksamrarn, S., Komutiban, O., Ratananukul, P., Chimnoi, N., Lartpornmatulee, N., Suksamrarn, A. (2006). Cytotoxic prenylated xanthones from the young fruit of *Garcinia mangostana*. *Chemical and Pharmceutical Bulletin*. 54, 301–305.

Suksamrarn, S., Suwannapoch, N., Phakhodee, W., Thanuhiranlert, J., Ratananukul, P., Chimnoi, N., Suksamrarn, A. (2003). Antimycobacterial activity of prenylated xanthones from the fruits of *Garcinia mangostana*. *Chemical and Pharmceutical Bulletin.* 51, 857–859.

Sultanbawa, M.U.S. (1980). Xanthonoids of tropical plants. *Tetrahedron*. 36, 1465–1506.

Summerbell, R. C. (1997). Epidemiology and ecology of onychomycosis. *Dermatology*. 194, 32-36.

Sundaram, B. M., Gopalakrishnan, C., Subramanian, S., Shankaranarayanan, D., Kameswaran, L. (1983). Antimicrobial activities of Garcinia mangostana. *Planta Medica*. 48, 59–60.

Tanaka, K., Hasegawa, J., Asamitsu, K., Okamoto, T. (2007). *Magnolia ovovata* extract and its active component magnolol prevent skin photoaging via inhibition of nuclear factor κB. *European Journal of Pharmacology*. 565(1-3), 212-219.

Taylor, W. C., Mangostin, G. (2006). Prenylated xanthones as potential antiplasmodial substances. *Planta Medica*. 72, 912–916.

Thring, T. S. A. Hili, P., Naughton, D. P. (2009) Anti-collagenase, anti-elastase and anti-oxidant activities of extracts from 21 plants. *BMC Complementary and Alternative Medicine*. 9(27): 1-11.

Thring, T. S. A., Hili, P. and Naughton, D. P. (2011). Antioxidant and potential anti-inflammatory activity of extracts and formulations of white tea, rose, and witch hazel on primary human dermal fibroblast cells. *Journal of Inflammation*. 8(27), 1-7.

Tomaino, A., Cristani, M., Cimino, F., Speciale, A., Trombetta, D., Bonina, F., Saija, A. (2006). In vitro protective effect of a Jacquez grapes wine extract on UVB-induced skin damage. *Toxicology In Vitro*. 20, 1395-1402.

Tsukahara, K., Nakagawa, H., Moriwaki, S., Takema, Y., Fujimura, T., Imokawa, G. (2006). Inhibition of ultraviolet-B-induced wrinkle formation by an elastase-inhibiting herbal extract: implication for the mechanism underlying elastase-associated wrinkles. *International Journal of Dermatology*. 45, 460–468.

Tur, E.(2007). *Environmental Factors in Skin Disease*. Switzerland: Karger.

Uttara, B., Singh, A. V., Zamboni, P. and Mahajan, R. T. (2009). Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. *Current Neuropharmacology*. 7(1), 65-74.

Van Mart, H. E., Steinbrink, D. R. (1981). A continuous spectrophotometric assay for *Clostridium histolyticum* collagenase. *Analytical Biochemistry*. 113, 356-365.

Varani, J., Warner, R. L., Gharaee-Kermani, M. (2000). Vitamin A antagonizes decreased cell growth and elevated collagen-degrading matrix metalloproteinases and stimulates collagen accumulation in naturally aged human skin. *The Journal of Investigative Dermatology*. 114, 480-486.

Vedamurthy, M. (2006) Antiaging therapies. *Indian Journal of Dermatology, Venereology and Leprology*. 72, 183-186.

Vlietinck, A., De Bruyne, T., Apers, S., Pieters, L. (1998). Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection. *Planta Medica*. 64, 97–109.

Wang, L. and Weller, C. L. (2006). Recent advances in extraction of nutraceuticals from plants. *Trends in Food Science and Technology*. 17, 300-312.

Wang, Y., Xia, Z., Xu, J. R., Wang, Y. X., Hou, L. N., Qiu, Y., Chen, H. Z. (2012). α-mangostin, a polyphenolic xanthone derivative from mangosteen, attenuates β-amyloid oligomers-induced neurotoxicity by inhibiting amyloid aggregation. Neuropharmacology. 62, 871–881.

Weecharangsan, W., Opanasopit, P., Sukma, M., Ngawhirunpat, T., Sotanaphun, U., Siripong, P. (2006). Antioxidative and neuroprotective activities of extracts from the fruit hull of mangosteen (*Garcinia mangostana* Linn.). *Medical principles and Practice*. 15, 281–287.

Wen, K. C., Fan, P. C., Tsai, S. Y., Shih, I. C., and Chiang, H. M. (2012). *Ixora parviflora* Protects against UVB-Induced Photoaging by Inhibiting the Expression of MMPs, MAP Kinases, and COX-2 and by Promoting Type I Procollagen Synthesis. *Evidence-Based Complementary and Alternative Medicine*. Article ID 417346, 1-11.

Wenas, D. M., Jufri, M., Elya, B. (2015). Formulation and Penetration Study of Liposome Xanthone of Mangosteen Pericarp Methanol Extract (*Garcinia* *mangostana* L.). *International Journal of Scientific and Research Publications*. 5(12), 434-439.

Williams, P., Ongsakul, M., Proudfoot, J., Croft, K., Beilin, L. (1995). Mangostin inhibits the oxidative modification of human low density lipoprotein. *Free Radical Research*. 23, 175–184.

William Reed Business Media (2013, Feb 07). Global cosmeceutical market set to grow with Asia showing most potential. *Cosmetics design-asia.com*. Retrieved Oct 22, 2014, from http://www.cosmeticsdesign-asia.com/Market-Trends/Global-cosmeceutical-market-set-to-grow-with-Asia-showing-most-potential

Wlaschek, M., Tantcheva-Poor, I., Naderi, L., Ma, W., Schneider, L. A., Razi-Wolf, Z., Schuller, J., Scharffetter-Kochanek, K. (2001). Solar UV irradiation and dermal photoaging. *Journal of Photochemistry and Photobiology*. 63, 41-51.

Yang, C. H., Li, M., Wei, Z. P., Han, F., and Gao, J. (2012). Advances in Isolation and Synthesis of Xanthone Derivatives. *Chinese Herbal Medicines*. 4(2), 87-102.

Yao, J., Liu, Y., Wang, X., Shen, Y., Yuan, S., Wan, Y., Jiang, Q. (2009). UVB radiation induces human lens epithelial cell migration via NADPH oxidase-mediated generation of reactive oxygen species and up-regulation of matrix metalloproteinases. *International Journal of Molecular Medicine*. 24(2), 153–159.

Yodhnu, S., Sirikatitham, A., Wattanapiromsakul, C. (2009). Validation of LC for the determination of alpha-mangostin in mangosteen peel extract: a tool for quality assessment of Garcinia mangostana L. *Journal of Chromatographic Science*. 47(3), 185-189.

Yoo, J. H., Kang, K., Jho, E. H., Chin, Y. W., Kim, J., Nho, C. W. (2011). α- and γ-mangostin inhibit the proliferation of colon cancer cells via β-catenin gene regulation in Wnt/cGMP signalling. *Food Chemistry*. 129, 1559–1566.

Yoshikawa, M., Harada, E., Miki, A., Tsukamoto, K., Si Qian, L., Yamahara, J., Murakami, N. (1994). Antioxidant constituents from the fruit hulls of mangosteen (*Garcinia mangostana* L.) originating in Vietnam. *Yakugaku Zasshi*. 114, 129–133.

Young, I. S. and Wooside, J. V. (2001). Antioxidants in health and disease. *Journal of Clinical Pathology*. 54(3), 176-186.

Yris, M. F., Carolina, D. C., Fabiana, T. M. C. V., Auro, N., Raquel, F. G., Maria, J. V. F. (2010). Protective effect of *Calendula officinalis* extract against UVB-induced oxidative stress in skin: evaluation of reduced glutathione levels and matrix metalloproteinase secretion. *Journal of Ethnopharmacology*. 127, 596–601.

Zarena, A. S., and Udaya Sankar, K. (2009). Supercritical carbon dioxide extraction of xanthones with antioxidant activity from Garcinia mangostana: Characterization by HPLC/LC-ESI-MS. *Journal of Supercritical Fluids*. 49, 330-337.

Zarena, A. S., and Udaya Sankar, K. (2011). Xanthones enriched extracts from mangosteen pericarp obtained by supercritical carbon dioxide process. *Separation and Purification Technology*. 80, 172-17.